REMARKS

I. Petition to Revive an Abandoned Application

In response to the "Notice of Abandonment" dated May 22, 2009 please consider and grant the accompanying "Petition to Revive an Abandoned Application". The delay in the response to the Office Action of November 12, 2009 was unintentional.

II. CLAIM CHANGES

Independent claims 36 and 41 for improvements in perishable cosmetic preparations and methods of preserving them have been amended to further distinguish their claimed subject matter from the prior art of record.

The bioactive glass particulates in the amended claims 36 and 41, which is the active preservative agent, now have particle sizes (d_{50}) of 10 µm or less. Unexpectedly improved properties as preservatives result from these smaller particle sizes. The fifth full paragraph on page 4 of the applicants' originally filed U.S. specification supports this limitation.

Dependent claims 41, 45, 47 and 48 have been limited to bioactive glass particulates with particle sizes (d_{50}) of 5 μm or less. The sixth full paragraph on page 4 of the applicants' originally filed specification supports this limitation.

The negative limitation regarding the toxic metal cations added to claims 36 and 41 is supported by the fourth paragraph on page 4 of the applicants' originally filed specification.

The limitation that the molar ratio limitation of calcium to phosphorus is greater than 2, which was added to claims 35 and 41, is supported by the fifth paragraph (last full paragraph) on page 3 of applicants' originally filed specification.

III. OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 36 and 37 were rejected on the ground of non-statutory obviousness-type double patenting (**ODP**) over claim 1 of US Patent 7,250,174 B2, in view of Greenspan (WO 98/11853) and Yli-Urpo, et al, US 5,762,950.

In accordance with 37 C.F.R. 1.321 a terminal disclaimer accompanies this amendment, which disclaims that portion of the term of any patent that issues from the above-identified U.S. Patent Application that exceeds the expiration date of US Patent 7,250,174 B2.

Accordingly withdrawal of the ODP rejection of claims 36 and 37 on the ground of non-statutory obviousness-type double patenting (**ODP**) over claim 1 of

US Patent 7,250,174 B2, in view of Greenspan (WO 98/11853) and Yli-Urpo, et al, US 5,762,950 is respectfully requested.

IV. OBVIOUSNESS REJECTION

Claims 36 to 48 were rejected as obvious under 35 U.S.C. 103 (a) over Shimono, et al (US 5,290,544), in view of Greenspan (WO 98/11853) and Yli-Urpo, et al (US 5,762,950).

A. The Claimed Invention

Claim 41 covers a preserved perishable cosmetic preparation in which a bioactive glass particulate is added and claim 36 claims a method of preserving by adding a bioactive glass particulate. Both claims now include the following limitations:

(1) the glass particulate is a bioactive glass;

(2) the particle size (d_{50}) is now reduced to **10 µm or less**;

(3) the bioactive glass contains Ca and P in a **molar ratio > 2** (a condition for formation of hydroxyapatite layer on contact with water);

(4) Ag^{+}, Cu^{+2}, Cu^{+} and Zn^{+} are now all **excluded** from the glass particulate;

(5) the cosmetic preparation contains from 0.1 to 25 wt. % of the bioactive glass pariculate.

Dependent claims 39, 45, 47 and 48 further limit the particle size of the bioactive glass particulate to 5 μm.

Dependent claims 37, 38, 43, and 44 are limited to preferred embodiments of bioactive glass compositions disclosed in the specification.

B. The Differences between the Claimed invention and the Prior Art

1. Shimono

The primary reference, Shimono, et al, has been described in detail in previous amendments. These descriptions are included here by explicit reference thereto.

The preserved cosmetic compositions of Shimono, et al, necessarily **include** one or more of the cations that are **excluded** by the new limitations added to the last paragraphs of independent claims 36 and 41. The sole independent claim of Shimono covers a cosmetic composition including a soluble glass particulate that must contain Ag^{+} cations, which are the active preservative agent in the composition, as explained in the specification of Shimono. The specification of Shimono teaches that a soluble glass containing at least one of Ag^{+}, Cu^{+2}, Cu^{+} and Zn^{+} will be effective as a preservative agent for a perishable cosmetic composition. **These toxic cations**, especially the silver cation, have now been **excluded** from the applicants' claimed cosmetic composition and method of preservation. Applicants' specification teaches that it is preferable to

exclude these toxic cations (4th full paragraph on page 4 of the applicants' specification).

In addition, applicants' claimed cosmetic composition and method of preservation require that the molar ratio of Ca to P must be greater than 2, which is a necessary condition for forming the hydroxyapatite layer. Shimono does disclose glass compositions that contain both Ca and P, but does not disclose the limitation that the molar ratio of Ca to P must be greater than 2 or that a hydroxyapatite layer is formed in contact with water. Examples 2 and 4 in columns 4 and following of Shimono do include both Ca and P but the molar ratio of Ca to P is << 1 in the case of each of these examples.

Furthermore the mechanism of action of the soluble glass preservative of Shimono is entirely different from that of the applicants' bioactive glass preservative because of the differences in their chemical compositions. The bactericidal action of the Shimono glass is based on the release of silver cations or one of the other toxic metal cations of Shimono (column 2, lines 3 to 25, of Shimono). In contrast the bactericidal action of the applicants' bioactive glass, which does not include any of the toxic metal cations, is based on the exchange of hydrogen cations in water that contacts the bioactive glass with sodium and calcium ions, which results in accumulation of sodium and calcium hydroxide near the surface of the bioactive glass and the formation of a hydroxyapatite layer on the surface of the bioactive glass (see page 3 of the applicants' originally filed US specification).

The observations on page 6 of the Office Action regarding the disclosures of preferred particle sizes in Shimono are somewhat misleading. Column 2, lines 45 to last line, teaches that their soluble glass may be added to cosmetic compositions that do not contain water, such as a powdery foundation. In that case it is preferable to pulverize the soluble glass so that it has an average particle size of 20 microns, preferably 5 microns – for "sufficiently mixing" (see column 2, line 61, of Shimono et al). The Shimono reference goes on to state that

> **"in the case when the cosmetic products are those containing water in the recipe, such as liquid foundation, skin location, milky lotion, shampoo, hair rinse, etc., the cosmetic products may be manufactured by crushing the soluble glass into a bead having a particle size of about 2 to 10 mm". Note that "mm" means millimeters.**

In other words, for aqueous cosmetic compositions Shimono teaches that it is preferred to add the soluble glass as a granulate with an average grain size of **2 to 10 mm**.

The disclosure regarding particle size in Shimono merely provides preferred particle sizes that differ for the aqueous and non-aqueous solid or semisolid cosmetic compositions. Their preferred particle sizes for the two different types of cosmetic compositions are chosen solely on the basis of manufacturing considerations – sufficient mixing etc.

Shimono does **NOT** disclose or suggest that soluble glass particulates with smaller particle sizes are more effective bactericidal agents. This is evidenced by the fact that Shimono teaches that the preferred soluble glass

granulate has a particle size in the range of about 2 to 10 mm when adding the soluble glass to preserve a cosmetic composition containing water.

Please especially note that applicants' dependent claims 40 and 46 claim embodiments limited to liquid compositions containing water or alcohol and that for those compositions Shimono teaches that a soluble glass granulate should be used with a grain size of 2 to 10 mm.

2. Yli-Urpo

Yli-Urpo discloses a bioceramic delivery device useful for *in vivo* delivery of a bioactive compound containing (i) hydroxyapatite, (ii) at least one bioactive glass, bioactive glass ceramic or bioactive ceramic, and (iii) a bioactive (therapeutic compound).

However Yli-Urpo does **NOT** teach that the hydroxyapatite is formed *in situ* by a reaction of the bioactive glass with an aqueous medium as stated in the last paragraph on page 7 of the Office Action. The teaching at column 1, lines 25 to 28, does not mention hydroxyapatite. Yli-Urpo teaches that the hydroxyapatite included in their delivery device is separately synthesized by known techniques (column 3, lines 35 to 40). This is made even more apparent by the teaching in Yli-Urpo that their preferred bioactive glass contains three components SiO_2, Na_2O, and CaO (see column 3, lines 29 to 35, and fig. 1 of Yli-Urpo). If a bioactive glass is to produce a hydroxyapatite layer on contact with water it must contain phosphorus because hydroxyapatite contains phosphorus. In contrast applicants' claims require that the hydroxyapatite is produced on contact of the

bioactive glass with an aqueous media and that the hydroxyapatite contains phosphorus and that the molar ratio of Ca to P is greater than 2.

Furthermore Yli-Urpo provides evidence that the term "soluble glass" describes a glass that is different from a "bioactive glass". The phase diagram in fig. 1 of Yli-Urpo shows that soluble glasses containing SiO_2, Na_2O and CaO and bioactive glasses containing SiO_2, Na_2O and CaO have different chemical compositions (different relative amounts of the three ingredients) and thus are **different**. Thus Shimono does not disclose a glass particulate that would be considered a "bioactive glass" by one of ordinary skill in the art, because Shimono describes their glass as a "soluble glass".

3. Greenspan

The Greenspan reference has been described in detail in previous amendments. These descriptions are included here by explicit reference thereto.

Greenspan does disclose applicants' preferred bioactive glass compositions of dependent claims 37 and 43 (page 10 to 11), but for a composition for wound healing, especially under battlefield conditions that necessarily include an antibiotic as well as bioactive glass. The primary function of the bioactive glass in the wound is to activate various growth factors due to increase of pH and release of sodium so as to allow the antibiotic to function. That is the combination of the bioactive glass and antibiotic provides a synergistic effect for wound healing (page 12, lines 12 to 19).

Greenspan also teaches that the preferred and recommended particle sizes for their bioactive glass should be less than 90 microns on page 11, lines 3 and 4. However the reason given is that the larger particles may induce an undesirable immune responds when the preparation is applied to an open wound at page 11, line 7.

Thus the preferred particle sizes for a different application not involving wound healing, such as the preservation of a cosmetic composition, are **NOT** disclosed or suggested by Greenspan. One skilled in the art would not find that the preferred particle sizes for an entirely different application from the application of Greenspan, wound healing, would be predictable from the disclosures regarding wound healing.

C. Rationale for the Obviousness Rejection

A prior art reference that contains teaching of doing the opposite from the claimed invention should not be employed alone or in combination with other prior art references to reject the claimed invention as obvious under 35 U.S.C. 103 (a). For example, see M.P.E.P. 2145. X. and the Federal Circuit Court of Appeals has said:

> "In determining whether such a suggestion [of obviousness] can fairly be gleaned from the prior art...It is indeed pertinent that these references teach against the present invention. Evidence that supports, rather than negates, patentability must be fairly considered." ***In re Dow Chemical Co.,*** 837 F.2nd 469,473, 5 U.S.P.Q.2d 1529, 1532 (Fed.Cir. 1988)

Shimono teaches the opposite from the invention claimed in the amended independent method claim 36 and in the amended independent composition claim 41, because these claims now exclude the primary active ingredients, namely the toxic metal cations, from the claimed cosmetic composition and method in these claims.

Also Shimono teaches the opposite from dependent method claim 40 and dependent composition claim 46 because Shimono recommends a particle size of from 2 to 10 mm for liquid cosmetic compositions, especially containing water, as noted above.

The basic rationale for the obviousness rejection in the paragraph bridging pages 8 and 9 of the Office Action (as best understood) is that one skilled in the art would be motivated to replace the soluble glass particulates of Shimono in their preserved cosmetic compositions with the bioactive glass particulate according to pages 10 to 11 of Greenspan because the particle size of the compositions of Greenspan allows them to be included in any cosmetic composition.

First the motivation for the replacement seems to contradict common sense because it would not be impossible to mix a particulate that has a 1 mm average particle size with any cosmetic composition including anhydrous compositions, such as foundation powder and lipstick, at least when the lipstick was formed.

Second the proposed modification would change the principle of operation of the primary reference, Shimono, which is **NOT** permitted under 35 U.S.C. 103 (a). See M.P.E.P. 2143.01 and *In re Ratti* 123 USPQ 349 (CCPA 1959). The principle of operation is changed by the proposed modification, because the mechanism of action of the bioactive glass of the claimed invention and Greenspan is fundamentally different from the mechanism of action of the soluble glass of Shimono. The soluble glass of Shimono operates by dispensing **toxic** metal cations, such as Ag^{+}, from their soluble glass particulate when it is in contact with water. In contrast, as explained above, the applicants' bioactive glass and the glass of Greenspan, is based on the exchange of hydrogen cations in water that contacts the bioactive glass with sodium and calcium ions, which results in accumulation of sodium and calcium hydroxide near the surface of the bioactive glass so that the pH increases and the formation of a hydroxyapatite layer on the surface of the bioactive glass. The mechanism of Shimono cannot occur in the applicants' bioactive glass because the toxic metal cations are now excluded from the bioactive glass of claims 36 and 41.

Accordingly the bioactive glass of Greenspan provides anti-bacterial action by means of an entirely different mechanism than the soluble glass of Shimono, so that replacement of the soluble glass particulate of Shimono with the bioactive glass particulate of Greenspan changes the principle of operation of the preservative agent.

Also Shimono contains the above-mentioned teaching of doing the opposite from the claimed invention.

Thus a case of *prima facie* obviousness cannot be based on a combination of the disclosures of Shimono and Greenspan with or without Yli-Urpo.

D. The Examiner's Response to Prior Arguments

The bioactive glass composition disclosed on pages 10 and 11 of Greenspan would **NOT** have all the same properties as the bioactive glass composition recited in claim 37 and 43 **if** the particle sizes of the bioactive glass particulates of the applicants' bioactive glass composition and and Greenspan's bioactive glass **are different**.

Applicants' second Declaration filed on August 15, 2008 and applicants' first Declaration filed in 2004 tested the ability of the bioactive glass particulates of the applicants' invention to inhibit the growth of or kill five common bacteria or other microbes inoculated into an aqueous culture medium (KBE). The results showed the **rate** of killing or inhibiting depended on the bioactive glass average particle size in all but one out of five cases.

The fundamental principle mentioned in the paragraph bridging pages 9 to 10 is true for many equilibrium properties that depend solely on molecular structure but not for all properties, for example properties that depend on the average particle size of a particulate of a given chemical composition.

In other words, the ratio of killing or inhibiting bacteria or microbes depends on the average particle size of the bioactive glass particulate as well as

the composition of the glass particulate. However this is exactly the crucial property for a bactericidal agent because the longer a bacteria remains in an initially inoculated cosmetic composition, the more damage it will do by consuming any organic species that are present.

E. The Unexpected Results in the Declarations are not Obvious from the Prior Art of Record

Applicants' claimed method and claimed composition are now limited to containing a bioactive glass particulate that has a particle size of up to about 10 microns. Applicants' claim preferred embodiments in which the particle size is 5 microns or less in their dependent claims 47 and 48.

The aforesaid first and second Declarations show that bioactive glass particulates as claimed in applicants' claims are increasingly more effective in inhibiting and killing bacteria and other microbes as their particle size decreases from 10 μm, to 4 μm, to 2 μm. The particulates, which have the same composition as the glass of Greenspan and a particle size of from 150 to 600 μm, **are ineffective** at inhibiting growth of at least two tested microbes (*E. Coli* and *A. Niger*) and poor at inhibiting the growth of one tested microbe (*C. Albicans*).

The results of the Declaration showed unexpectedly that the particulates became significantly more effective when their particle size was 10 μm or less in comparison to over 100 μm. Also they showed that the particulates with a particle

size around 5 μm were somewhat more effective than the particulates with a particle size of 10 μm.

Neither Shimono nor Greenspan teach that bioactive glass particulates become more effective at killing and inhibiting bacteria as their particle size decreases.

Greenspan on page 11 does teach that particle sizes less than 90 μm are recommended and that particle sizes less than 10 μm may be used. But Greenspan does not state that the smaller particle sizes are more effective as bacteriostatic agents. Greenspan only states that the large particle sizes have the problem that they produce an undesirable immune reaction when their composition for healing wounds is placed in a wound (page 11, line 7).

Naturally if the particle size of the bioactive glass is optimized for healing wounds in a wound healing composition, one skilled in the art would not expect that the same preferred range would result for preservation of a cosmetic composition. The applications are different so that the preferred particle size range for one application is not necessarily the same as for the other application. One skilled in the art would not be able to predict that the optimum particle size for inhibiting or killing bacteria would be the same as the optimum particle size for use in the wound healing composition of Greenspan. Predictability is required for an obviousness rejection under the newer rationale.

Thus Greenspan does **not** anticipate the unexpected results of the Declaration: Greenspan does not teach or suggest that the recited bioactive glass composition on pages 10 and 11 is unexpectedly faster and more effective

at killing bacteria or microbes in a cosmetic composition (without an antibiotic as required in the wound healing composition) when its particle size is 10 μm or less.

The results of the Declarations can also not be anticipated by Shimono because Shimono implies that a glass with a particle size of 2 to 10 millimeters is more or less as effective as a particulate with a particle size of 5 μm or less at column 2, line 56 to 68. Applicants would add the particulates with the smaller particle size to both liquid cosmetic compositions and to solid cosmetic compositions on the basis of the results of their Declaration that shows that the smaller particle sizes are much faster and more effective at killing and inhibiting bacteria. However Shimono is clearly unaware of this effect or he would not suggest using such large grain sizes for the liquid cosmetic compositions. They use the smaller particle sizes for cosmetic powders because of the convenience of easy and rapid mixing with the powders.

Furthermore Shimono does not disclose a bioactive glass particulate only a soluble glass particulate and Yli-Urpo teaches that the two different glass particulates are different with different compositions and thus would not be expected to have the same properties including optimum particle size ranges.

In addition applicants' claims have now been amended to recite glass particulates that have clearly different glass compositions, which would not be expected to have the same properties, from those of Shimono. The applicants' claimed compositions now exclude the toxic metal cations that are the effective ingredients in Shimono and also must have a certain molar ratio of Ca to P (and

thus must contain both Ca and P). Thus one could not predict the unexpected results of the applicants' Declarations from the disclosures of Shimono, since the glass compositions are different as well as the particle size results. Furthermore Shimono is silent regarding the effect of particle size on effectiveness as a bactericidal agent.

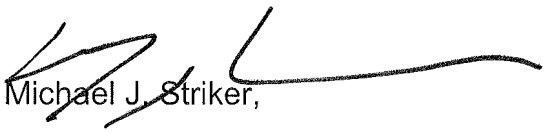
The results in the two Declarations would overcome any case of *prima facie* obviousness based on the subject matter of Shimono, Greenspan and Yli-Urpo. However it is also respectfully submitted that these three prior art references do NOT establish a case of *prima facie* obviousness of the applicants' invention, especially as claimed in the above amended claims.

For the aforesaid reasons and because of the changes in the claims, withdrawal of the rejection of claims 36 to 48 as obvious under 35 U.S.C. 103 (a) over Shimono, et al (US 5,290,544), in view of Greenspan (WO 98/11853) and Yli-Urpo, et al (US 5,762,950) is respectfully requested.

Should the Examiner require or consider it advisable that the specification, claims and/or drawing be further amended or corrected in formal respects to put this case in condition for final allowance, then it is requested that such amendments or corrections be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing the case to allowance, he or she is invited to telephone the undersigned at 1-631-549-4700.

In view of the foregoing, favorable allowance is respectfully solicited.

Respectfully submitted,



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